REMARKS

Applicants hereby submit that the enclosures fulfill the requirements under 37 C.F.R. §1.821-1.825. The amendments in the specification merely insert the paper copy of the Sequence Listing and sequence identifiers in the specification. No new matter has been added.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment.

Please apply any further necessary charges and apply all credits to Deposit Account No. 06-1050.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at (858) 678-5070.

Respectfully submitted,

Date: Nov. 01, 2001

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"Version With Markings to Show Changes Made"

Applicant : Hynda Kleinman et al. Art Unit : 1643
Serial No. : 09/772,445 Examiner : Unknown
Filed : January 29, 2001
Title : THYMOSIN BETA4 PROMOTES WOUND REPAIR

In the specification:

Paragraph beginning at page 3, line 19, has been amended as follows:

In a first embodiment, the invention provides a method for promoting wound repair in a subject in need of such treatment by administering to the subject or contacting the site of the wound with a wound-healing effective amount of a composition containing a wound healing polypeptide comprising the amino acid sequence LKKTET (SEQ ID NO:1) and conservative variants thereof having wound healing activity. In one aspect of the method, the wound healing polypeptide is Tβ4 or an isoform of Tβ4.

Paragraph beginning at page 3, line 26, has been amended as follows:

In another embodiment, the invention provides a method for promoting tissue repair in a tissue in need of such treatment by contacting the tissue with an effective amount of a composition containing a wound healing polypeptide comprising the amino acid sequence LKKTET (SEQ ID NO:1) and conservative variants thereof having wound healing activity, or nucleic acid encoding a wound healing polypeptide. In one aspect of the method, a wound healing peptide is Tβ4 or an isoform of Tβ4. The tissue may be contacted either *in vivo* or *ex vivo*.

Paragraph beginning at page 4, line 4, has been amended as follows:

In yet another embodiment, the invention provides a method of modulating wound repair in a subject in need of such treatment by systemic delivery of a wound-healing effective amount of a wound healing polypeptide comprising the amino acid sequence LKKTET (SEQ ID NO:1) and conservative variants thereof having wound healing activity. In one aspect of the method, a wound healing peptide is Tβ4 or an isoform of Tβ4.

Paragraph beginning at page 4, line 21, has been amended as follows:

In yet another embodiment, the present invention provides pharmaceutical compositions comprising a wound healing polypeptide comprising the amino acid sequence LKKTET (SEQ ID NO:1) and conservative variants thereof having wound healing activity and a pharmaceutically acceptable carrier. In one aspect, the wound healing polypeptide is Tβ4 or an isoform of Tβ4.

Paragraph beginning at page 6, line 21, has been amended as follows:

FIG. 10 shows an amino acid sequence of Tβ4 (SEQ ID NO:2).

Paragraph beginning at page 6, line 22, has been amended as follows:

FIG. 11 shows the amino acid sequence of several known isoforms of Tβ4, and their phylogenetic distribution (SEQ ID NOs:2 through 15, respectively). N-terminal acetylation is indicated by □ac.□ Residues between 13 and 24 are thought to be important for actin binding.

Paragraph beginning at page 9, line 21, has been amended as follows:

Tβ4 isoforms have been identified and have about 70%, or about 75%, or about 80% or more homology to the amino acid sequence of Tβ4 set forth in Fig. 10. Such isoforms include, for example, $T\beta4^{ala}$, Tβ9, Tβ10, Tβ11, Tβ12, Tβ13, Tβ14 and Tβ15 (Fig. 11; see also, Mihelic *et al.*, (1994) *Amino Acids*, 6:1-13, which describes the amino acid sequence of other Tβ4 isoforms, and is incorporated herein by reference). Similar to Tβ4, the Tβ10 and Tβ15 isoforms have been shown to sequester actin. Tβ4, Tβ10 and Tβ15, as well as these other isoforms share an amino acid sequence, LKKTET (SEQ ID NO:1), that appears to be involved in mediating actin sequestration or binding. Although not wishing to be bound to any particular theory, the wound healing activity of Tβ4 and Tβ4 isoforms may be due, in part, to the ability to polymerize actin. For example,Tβ4 can modulate actin polymerization in wounds to promote healing (*e.g.*, β-thymosins appear to depolymerize F-actin by sequestering free G-actin). Tβ4's ability to modulate actin polymerization may therefore be due to all, or in part, its ability to bind to or sequester actin via the LKKTET (SEQ ID NO:1) sequence. Thus, as with Tβ4, other proteins

which bind or sequester actin, or modulate actin polymerization, including Tβ4 isoforms having the amino acid sequence LKKTET (SEQ ID NO:1), are likely to promote wound healing alone, or in a combination with Tβ4, as set forth herein.

Paragraph beginning at page 10, line 16, has been amended as follows:

In addition, other proteins having actin sequestering or binding capability, or that can mobilize actin or modulate actin polymerization, as demonstrated in an appropriate sequestering, binding, mobilization or polymerization assay, or identified by the presence of an amino acid sequence that mediates actin binding, such as LKKTET (SEQ ID NO:1), for example, can similarly be employed in the methods of the invention. Such proteins include gelsolin, vitamin D binding protein (DBP), profilin, cofilin, depactin, DNaseI, vilin, fragmin, severin, capping protein, β-actinin and acumentin, for example. As such methods include those practiced in a subject, the invention further provides pharmaceutical compositions comprising gelsolin, vitamin D binding protein (DBP), profilin, cofilin, depactin, DNaseI, vilin, fragmin, severin, capping protein, β-actinin and acumentin as set forth herein. Thus, the invention includes the use of wound healing polypeptide comprising the amino acid sequence LKKTET (SEQ ID NO:1) and conservative variants thereof.

In the claims:

Claim 1 has been amended as follows:

1. (Amended) A method for promoting wound healing in a subject in need of such treatment comprising administering to the subject a wound-healing effective amount of a composition containing a wound healing polypeptide comprising the amino acid sequence LKKTET (SEQ ID NO:1) and conservative variants thereof having wound healing activity.